

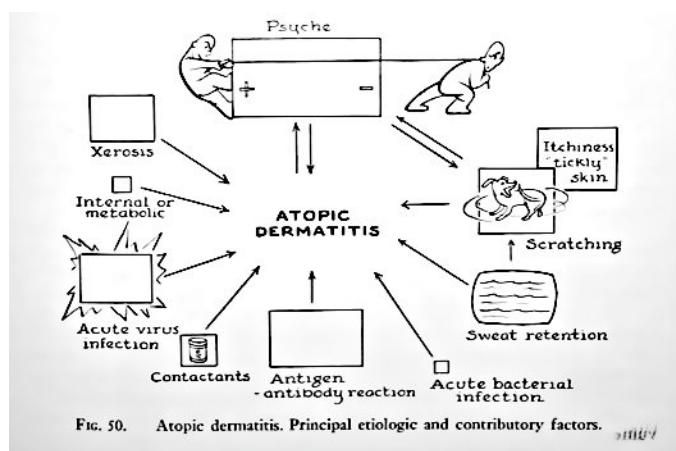
Advanced Therapeutics: Managing the Severe and Refractory Eczema Patient

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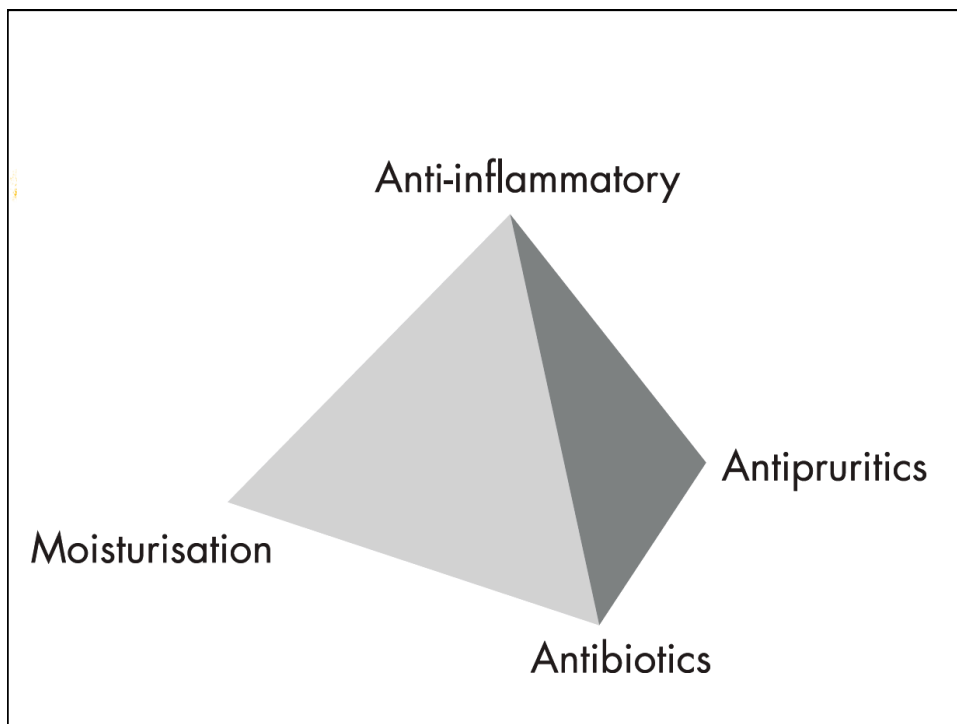
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Pillsbury DM, Kligman AM, Shelley WB. *A manual of cutaneous medicine*, by Donald M. Pillsbury, Walter B. Shelley [and] Albert M. Kligman. Philadelphia. Saunders, 1961.



Diagnostic Considerations

QUESTION: Foods and AD

- How do you assess the contribution of food allergy (FA) in severe eczema?

FA and AD

- FA and AD are highly associated.
 - Up to 37% of children <5 years with moderate to severe AD will have IgE-mediated FA
- Whether FA can exacerbate AD is controversial (lack of well-designed avoidance trials in patients with AD)
 - Several studies found improvement in pruritus when patients with egg allergy and AD were placed on egg-free diet

Lever R et al, Pediatr Allergy Immunol 1998

FA and AD misconceptions

- Eczematous flares can be erroneously attributed to foods by patient/parent
 - May be precipitated by irritants, humidity, change in temperature, infections
- Thus, AD may continue to flare in patients with FA despite strict elimination diet

Practical considerations: when to consider testing to foods in AD

- When proper skin care is not working in child
- When eczema flares are consistently associated with a specific food as a trigger
- If the child is not growing well

*Milk, egg, and peanut are the most common allergens in young children (*test judiciously*)

****The younger the child and the more severe the AD, the greater likelihood that child has FA***

Guillet G & MH, Arch Dermatol 1992

QUESTION: Foods and AD

- If you eliminate a food (e.g. eggs or milk) for a period of time to see if it is contributory, are you increasing the risk of *anaphylaxis* when you reinstitute that same food?

QUESTION: Foods and AD

Actually 2 questions:

- If you eliminate a food (e.g. eggs or milk) for a period of time to see if it is contributory, what is the risk of *a reaction* when you reinstitute that same food?
- What are the risks for a severe reaction or *anaphylaxis*?

Factors to consider before reintroducing foods

- Has food elimination helped AD?
- How long has food been eliminated?
- How long/frequently was food in diet prior to elimination? (Is this an infant or teenager?)
- Has testing been performed? If so, results?

*When tolerance develops to food, reintroduction of food will NOT cause AD to recur or worsen.

Sampson & Scanlon, J Peds 1989

- 75 children (3-18 mos) with AD diagnosed with FA using DBPCFC
- Milk, peanut, egg most common
- Allergen-restricted diet for 1-2 years → repeat DBPCFC: 31% FA resolved
- Patients with both skin + resp sx at initial OFC were *less* likely to have resolved FA
 - compared to those with skin only or skin + GI sx

Risk factors for severe food reactions

- Asthma!
- Amount of allergen ingested
- Form of food (raw, cooked, processed)
- Age of patient (teen, young adult)
- Degree of sensitization (threshold dose) at time of ingestion
- Rate of absorption (empty stomach, exercise, alcohol intake, etc)

QUESTION: Foods and AD

- What is the status of food patch testing in severe AD? Is there any role for it in refractory cases, wherein food-specific IgE-guided diet manipulation has already been attempted but with limited success?

Atopy Patch Test (APT)

- 2010 Food Allergy Guideline 8: NIAID-sponsored EP suggests that APT should not be used in routine evaluation of non-contact FA
 - No standard reagents available
 - No studies that specifically address APT methodology met inclusion criteria for report
 - Two large studies conclude there is no significant clinical value in using APTs for FA diagnosis
- Mehl et al, JACI 2006 & Keskin et al, Ann Allergy Asthma Immunol 2005

QUESTION: Foods and AD

- Effect of super high IgEs on specific positive predictive value for milk, eggs, etc.?
- How to interpret without challenge?

“Super high” IgE levels

- Elevated total IgE levels frequently found in atopic individuals
- No studies to date provide support of use of total IgE in interpreting specific IgE levels
- Predictive value of ratio of sIgE to total IgE compared with DBPCFC for diagnosis of FA.
Conclusion: Ratio offers **no** advantage over sIgE alone.

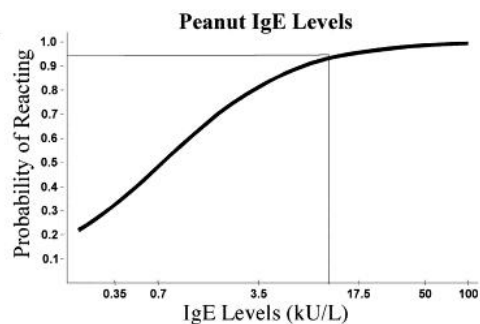
Mehl A et al, Allergy 2005

Predictive value of food allergen-specific IgE levels

95% Predictive Level		
Allergen	[kU _A /L]	PPV
Egg	7	98
- Infants ≤ 2 yrs ⁺	2	95
Milk	15	95
- Infants ≤ 2 yrs ⁺⁺	5	95
Peanut	14	100
Fish	20	100
Tree nuts ⁺⁺⁺	~15	~95
Soybean	30	73
Wheat	26	74

+ Boyano MT, et al. Clin Exp Allergy 2001; 31(9):1464-9.
 ++ Garcia-Ara C, et al. J Allergy Clin Immunol 2001; 107(1):185-90.
 +++ Clark AT, Ewan P. Clin Exp Allergy. 2003; 33(8):1041-5

PPV = Positive predictive value



Increasing probability of clinical reactivity with increasing level of food-antigen specific IgE value; note: values <0.35 do not exclude allergic reactivity



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[Journal of Allergy and Clinical Immunology 2004; 113:805-819](#)

QUESTION: Infections

- Is there any role for skin culture, as opposed to empiric use of anti-staphylococcal systemic antibiotics in severe AD flares?
- Occasional furuncle or recurrent clinical staph infections w/o infections, IgE > 10,000. No family history of Hyper IgE syndrome?

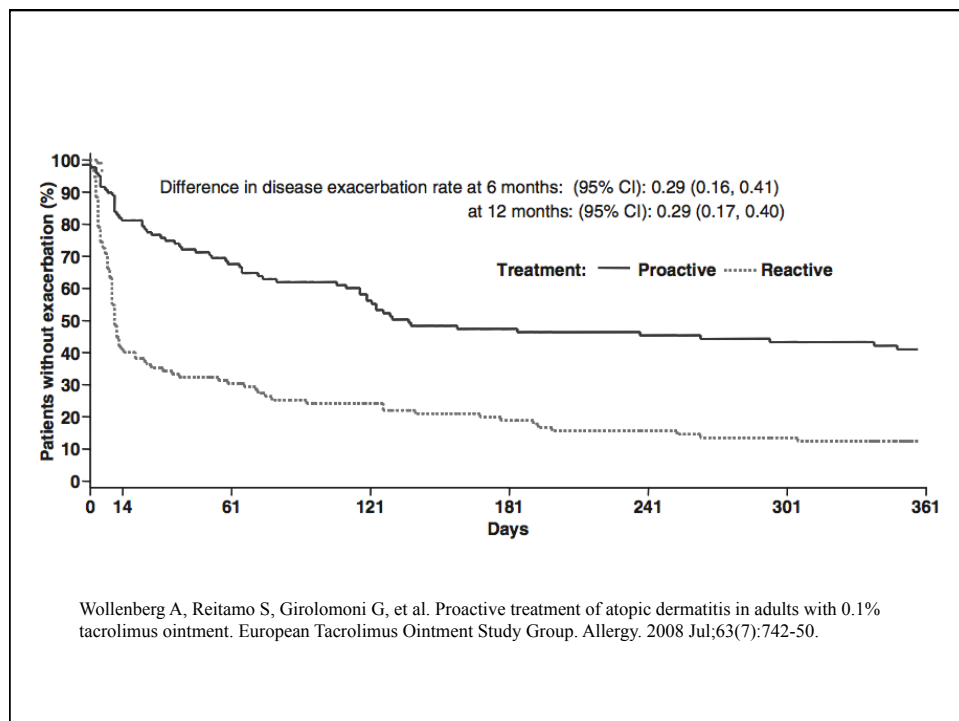
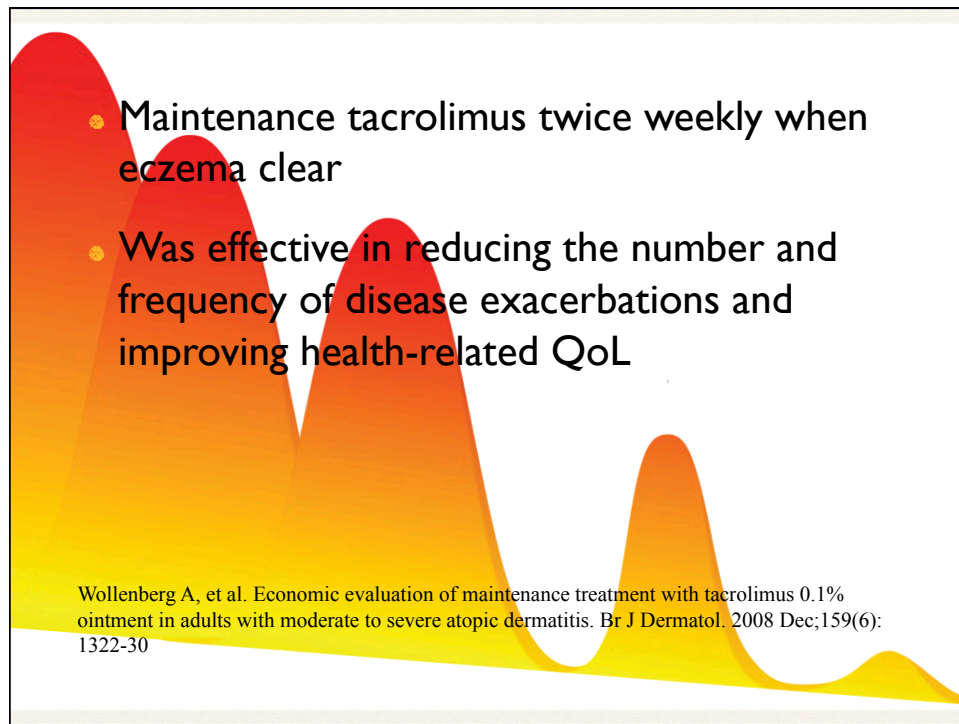
Infections

- Staph is incredibly common (> 90% in severe cases)
- Usually I do not culture anymore
- For some reason, MSSA > MRSA in this group so far...
- But in refractory cases, or if pustules or ulcers, culture could be important, esp immunosuppressed patients... so common, however

Therapeutics

QUESTION: TCIs

- How often is combination therapy with both a moderate potency corticosteroid and a topical immuno-modulator more helpful than either one alone?
- What is the most appropriate role for the use of calcineurin inhibitors?



Synergy

- I have used a topical steroid in the AM and then a TCI in the PM; for some cases of severe, refractory disease, I think there may be synergy
- Also a nice way to transition for patients who feel stinging and burning with TCIs
- “The results of our small retrospective study suggest that TCPO may be more effective than either 0.1% tacrolimus or clobetasol propionate 0.05% ointment monotherapy in the treatment of recalcitrant CLE.”

Madan V, August PJ, Chalmers RJ. Efficacy of topical tacrolimus 0.3% in clobetasol propionate 0.05% ointment in therapy-resistant cutaneous lupus erythematosus: a cohort study. Clin Exp Dermatol. 2010 Jan;35(1):27-30.

QUESTION: Phototherapy

- Some area dermatologists are still using UV radiation in the treatment of eczema, even in young children. What is the role of UV treatment?



Phototherapy



- 1903 Nobel Prize in Medicine: Niels Ryberg Finsen, Danish pioneer of phototherapy
- *Om Lysets Indvirkninger paa Huden* (On the effects of light on the skin)
- Probably multiple mechanisms including increasing vitamin D which in turn enhances cathelicidin

Phototherapy

- Works in about 60% of refractory cases
- NB-UVB (311nm) seems very safe

Problems:

- Time
- Money (co-pays, parking, etc)

Home units...

QUESTION: Topical Steroids

- What is the highest class of steroids for how long with what frequency is your top dose for kids?

Topical Steroids

- No easy answer here... to some extent, I will use whatever it takes, even class 1 steroids on the face for brief bursts
- Pearl: for patients saying “as soon as I stop, it come RIGHT BACK” or “I have to use EVERY DAY”, steroid potency is probably too low*

*Provided all other areas of the tetrad are being maximized, of course

QUESTION: Systemic Medications

- How long is your trial of cyclosporine?

Cyclosporine: From PeDRA

- Rapid
- 5mg/kg/d, 300mg/d max
- Monitoring: BP q wk x 4 then q mo CBC, LFTs, BUN, Cr, CMP, uric acid, lipids monthly x 3 then every 8 wks
- Maintain x 3 mo then taper
- Limit to 1 yr
- (Pediatric Dermatology Research Alliance)

Imuran: From PeDRA

- Onset is 4-6 weeks
- Can use concurrent pred x 1 mo
- Baseline TPMT if normal: 2.5-3.5 mg/kg/d
- If intermediate TPMT: 1mg/kg
- Monitoring: CBC, LFTs, BUN, Cr at 2,4,8,12 wks then every 8 wks
- Maintain x 3 mo then taper
- Limit to 2 yrs

QUESTON: Antibiotics

- When and how long to treat with antibiotics for chronic management?
- In recalcitrant patient, if staph superantigen can play a role, and skin has staph w/o clinical infection, any role to try and decrease staph load?

Antibiotics

- Since the Paller bleach bath study, I have used less topical and systemic antibiotics than ever
- Bleach baths: qd when flaring, biweekly as maintenance
- Staph is ubiquitous and, for some reason, MRSA seems to be a less common colonizer here; I usually do not culture anymore
- Cephalexin still seems to be most helpful
- Usually 14 days, though I have used TMP-SMX longer term in some severe cases

QUESTION: Yeast

- Recalcitrant patient and malassezia/pityrosporum - if no clinical infection, leave it alone? KOH prep? What if positive?

Yeast

- A few interesting papers on head and neck dermatitis in young adults showing that *Malassezia* allergy may play a role
- Consider: Itraconazole daily x 2 mo then long-term weekly treatment 100mg po qd
- This has not worked well for me... but I do try and I have had 2 patients respond well... and about 10 fail the treatment

Darabi K, et al. The role of *Malassezia* in atopic dermatitis affecting the head and neck of adults. *J Am Acad Dermatol*. 2009 Jan;60(1):125-36.

QUESTION: Pruritus

- What role if any for anti-anxiety meds, sleep aids in children with intractable scratching and sleeplessness?

Pruritus

- Data is poor that anti-pruritics help our more severe cases (I wish they did help!)
- Even in my severe cases, I usually am able to taper these off once skin is better
- Hydroxyzine in kids; doxepin or mirtazapine in older patients can really help get through the night due to sedative effects

QUESTION: Immunotherapy

- Immunotherapy to house dust mites (HDM)?
- How effective IT might be in bad AD?

Allergen Immunotherapy: 3rd update of practice parameter (2011)

- Summary Statement 8: There are some data indicating that immunotherapy can be effective for atopic dermatitis when associated with aeroallergen sensitivity
- Bussman et al, JACI 2007: In review of 4 placebo-controlled studies, statistical analysis showed significant improvement in symptoms in AD patients who received SCIT.

Subcutaneous immunotherapy (SCIT)

- Werfel T et al, Allergy 2006
 - Multi-center, randomized, double-blind study of 51 adults with AD
 - Maintenance doses of 20, 2000, and 20,000 SQ-U weekly for 1 year
 - HDM SCIT effectively reduced AD in dose-dependent manner, as measured by SCORAD and topical corticosteroid use

Subcutaneous immunotherapy (SCIT)

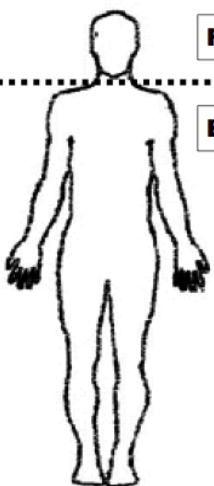
- Bussman et al, Clin Exp Allergy 2007
 - Open pilot study to evaluate the benefit of HDM SCIT x 6 mos in 25 AD patients with HDM sIgE
 - Subjective and objective SCORAD improved significantly within 4 weeks of treatment
 - IL-10 levels increased; CCL17 and IL-16 decreased
 - HDM IgE decreased while IgG4 increased

Sublingual immunotherapy (SLIT)

- Pajno et al, JACI 2007 (Italy)
 - Randomized, double-blind, placebo-controlled study of 48 children (5-16 years) with HDM sensitization and AD (SCORAD >7), stratified by disease severity
 - SLIT or placebo for 18 months + standard therapy
 - Significant difference in SCORAD and use of rescue meds found only in patients with mild-moderate AD
 - Severe patients had only marginal benefit
 - SLIT discontinued in 2 patients because of exacerbation of dermatitis

QUESTION: Compliance

- Logistics of lubricating school-aged child interfering with therapy?
- How to sort out all of these medications/ treatments?

ECZEMA ACTION PLAN				
<p>* A moisturizer is extremely important. We recommend Aveeno, Nouriva Repair, or Hydrolated Petrolatum twice per day for any patient with eczema.</p>		CLEAR	MILD-MOD	SEVERE
	FACE	AM	Moisturizer* Protopic ointment Hydrocortisone 2.5% oint.	Moisturizer* Hydrocortisone 2.5% oint. Bactroban oint.
	FACE	PM	Moisturizer* Protopic ointment Hydrocortisone 2.5% oint.	Moisturizer* Hydrocortisone 2.5% oint. Bactroban oint.
	BODY	AM	Moisturizer* May use Protopic ointment or Hydrocortisone 2.5% ointment to any small flare-ups for several days as needed or on the weekends.	Moisturizer* Triamcinolone oint. Fluocinonide oint. Bactroban oint. Call your doctor if not improving after 2 weeks
		PM	Moisturizer* May use Protopic ointment or Hydrocortisone 2.5% ointment to any small flare-ups for several days as needed or on the weekends.	Moisturizer* Triamcinolone oint. Fluocinonide oint. Bactroban oint. Bath with Balnetar oil Unna Boots Call your doctor if not improving after 2 weeks

Always check with your doctor before starting or changing any medications or if there are any questions or concerns.

Action Plan

AM:

1. Apply triamcinolone ointment to eczema areas
2. Apply moisturizer everywhere

During day:

1. Apply moisturizer everywhere 1-2 times

PM:

1. Dilute bleach bath for 10 minutes
2. Pat dry
3. Apply triamcinolone ointment to eczema areas
4. Apply moisturizer everywhere

Do this for several days (up to 1 week) until better. Once better...

QUESTION: Miscellaneous

- How to use wet wraps, and how safe are they?
- What is the “best” moisturizer?

Miscellaneous

- Wet wraps, bleach baths, unna boot instructions

www.eczemacarecenter.com

- The best moisturizer is one they will use...
- But... my favorites include the ones with ceramides since I think you can get similar effect to greasier products in less-greasy formulations

What to do when everything seems to fail...

Discussion...

THANK YOU!